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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/189,415	11/10/1998	BRETT B FINLAY	07422/013001	5485
500	7590	02/11/2004	EXAMINER	
SEED INTELLECTUAL PROPERTY LAW GROUP PLLC 701 FIFTH AVE SUITE 6300 SEATTLE, WA 98104-7092			DEVI, SARVAMANGALA J N	
		ART UNIT	PAPER NUMBER	
		1645	25	
DATE MAILED: 02/11/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/189,415	FINLAY ET AL.
Examiner	Art Unit	
S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 13 July 2001.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-59 is/are pending in the application.
- 4a) Of the above claim(s) 8-51 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-7 and 52-59 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>4-6</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Preliminary Amendments

- 1) Acknowledgment is made of Applicants' preliminary amendments filed 07/24/00 (paper no. 2) and 04/11/01 (paper no. 8). With this, Applicants have amended the specification.

Election

- 2) Acknowledgment is made of Applicants' election filed 03/28/00 (paper no. 13) in response to the restriction requirement mailed 01/14/00 (paper no. 7). Applicants have elected, with traverse, invention I, claims 1-7, drawn to Tir polypeptide. Applicants' traversal is on the grounds that a search for claims 23-28 in conjunction with claims 1-7 would not constitute an undue burden in view of the fact that the subject matter of the inventions I and V overlap. Applicants however agree that the polypeptide of invention I can have numerous uses in addition to those recited in claims 23-28.

Applicants' arguments have been carefully considered, but are non-persuasive. In the instant case, the restriction requirement follows all appropriate statutes and regulatory principles and conforms closely with guidelines provided by MPEP, Chapter 800. With regard to burden, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed, and (2) a serious search *and examination* burden is placed on the Examiner if restriction is not required. As Applicants readily acknowledge, in the instant case, the product of invention I is capable of separate use, i.e., as a source of coating antigenic reagent in an *in vitro* immunological assay to detect specific antibodies. Applicants have not presented any arguments showing that the claimed product cannot be used in a materially different non-immunization process. With regard to burden of search and examination, MPEP 803 states that a burden can be shown if the Examiner shows either separate classification, different file of search or separate status in the art. In the instant application, a burden has been established by showing that inventions I and V are classified under separate subclasses necessitating separate and non-coextensive searches of issued US patents under different subclasses. Clearly, different searches and issues are involved in the examination of each invention. For these reasons, the restriction set forth in the Office Action mailed 01/14/00 is proper and is hereby made FINAL.

Since Applicants have elected the product claims of invention I, the method of using the product claims of invention V would be kept pending, pursuant to the rejoinder provisions of M.P.E.P 821.04 and would be rejoined with the elected product claims if and when the latter were deemed allowable. *Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is*

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earlier. Amendments submitted after final rejection are governed by 37 C.F.R 1.116; amendments submitted after allowance are governed by 37 C.F.R 1.312. The requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 C.F.R 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. § 101, 102, 103 and 112. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See ‘Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C § 103(b),’ 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right rejoinder.

Status of Claims

- 3) New claims 52-59 have been added via the preliminary amendment filed 04/11/00.
Claims 1-59 are pending.
Claims 8-51 have been withdrawn from consideration as being directed to non-elected inventions. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.
Elected claims 1-7 and 52-59 are under examination. An Action on the Merits for these claims is issued in the instant Office Action (paper no. 25).

Sequence Listing

- 4) Acknowledgment is made of Applicants’ raw sequence listing which has been entered on 07/26/01 (paper no. 24).

Drawings

- 5) The drawings submitted in the instant application are objected to under 37 C.F.R 1.84 because of the reasons set forth by the Draftsperson in the attached Form PTO 948 (paper no. 25). Correction is required. Applicant is asked to note the changes effected 03 May 2001, particularly the changes to the ‘Timing of Corrections’:

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. *Correction of Informalities -- 37 C.F.R 1.85; 1097 O.G. 36*

New formal drawings must be filed with the changes incorporated therein. The art unit number, application number (including series code) and number of drawing sheets should be written on the reverse side of the drawings. Applicant may delay filing of the new drawings until receipt of the “Notice of Allowability” (PTOL-37 or PTO-37). If delayed, the new drawings MUST be filed

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within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability" to avoid extension of time fees. Extensions of time may be obtained under the provisions of 37 C.F.R. 1.136(a) for filing the corrected drawings (but not for payment of the issue fee). The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the three month shortened statutory period set in the "Notice of Allowability" (PTO-37). Within that three-month period, two weeks should be allowed for review of the new drawings by the Office. If a correction is determined to be unacceptable by the Office, Applicant must arrange to have an acceptable correction resubmitted within the original three-month period to avoid the necessity of obtaining an extension of time with extension fees. Therefore, applicant should file corrected drawings as soon as possible.

Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

Priority

- 6) The instant application claims priority to the Provisional of application SN 60/065,130 filed 11/12/1997.

Information Disclosure Statements

- 7) Acknowledgment is made of Applicants' Information Disclosure Statements filed 02/16/99, 05/07/99 and 10/12/99 (paper no. 4, 5 and 6). The information referred to therein has been considered and a signed copy is attached to this Office Action (paper no. 25).

Specification - Informalities

- 8) The specification is objected to for the following reason(s):

The use of the trademarks in the instant specification has been noted in this application. For example, see page 5, line 22; page 38, line 17; page 39, lines 8 and 19; page 40, line 21: 'Triton X-100'; page 46, line 13; page 47, line 24: 'Tween-20'; and page 49, line 4: 'Taq DyeDeoxy'.

Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification to make similar corrections to the trademarks, wherever they appear.

Rejection(s) under 35 U.S.C § 112, First Paragraph

- 9) Claims 1-5 and 52-59 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Instant claims broadly read on a substantially purified intimin-binding Tir polypeptide of any origin, any structure, and any size from any pathogen, any A/E pathogen, any strain or isolate of EPEC or EHEC, which Applicants are clearly not in possession of. The breadth of the claims encompasses a Tir polypeptide of microbial and non-microbial origin. The only Tir polypeptides of differing structure and properties disclosed within the instant specification are SEQ ID NO: 2 and SEQ ID NO: 4 from one isolate or strain of EPEC and EHEC respectively, one of which is recognizable by anti-phosphotyrosine antibodies and the other not so recognizable. The two Tir sequences SEQ ID NO: 2 and 4 vary in their structure or amino acid composition. Instant claims recite insufficient relevant identifying characteristics of the claimed Tir to allow one skilled in the art to predictably determine complete structures of other Tir polypeptide sequences from other strains of EPEC and EHEC, other A/E pathogens, other pathogenic or non-pathogenic microbes or organisms, absent further guidance. Since the claimed Tir polypeptide genus encompasses undisclosed Tir polypeptides from other strains of EPEC or EHEC, other A/E pathogens, other pathogenic or non-pathogenic microbes or organisms, already discovered and yet to be discovered, the disclosed Tir structural feature for one EHEC or EPEC species (strain) does not constitute a substantial portion of the claimed genus.

Therefore, the disclosure of a single EHEC Tir or EPEC Tir amino acid sequence from a single strain of EHEC or EPEC does not provide an adequate written description of the claimed Tir polypeptide genus, and in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that Applicants were in possession of the genus of Tir polypeptide as claimed. See Written Description Requirement published in *Federal Register*, Vol. 66, No. 4, Friday, 05 January 2001, Notices, p. 1099-1111.

- 10) Claims 1-5 and 52-59 are rejected under 35 U.S.C § 112, first paragraph, because the specification, while being enabling for a substantially purified EHEC or a EPEC Tir polypeptide of the amino acid sequence, SEQ ID NO: 2 or SEQ ID NO: 4, and a pharmaceutical composition comprising the same, does not reasonably provide enablement for a substantially purified generic Tir polypeptide of any origin, size or

structure and a pharmaceutical composition comprising the same that is 'suitable for treating a pathogenic infection, as claimed broadly. The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and/or use the invention commensurate in scope with these claims.

The instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant case, the two Tir polypeptides having the amino acid sequences of SEQ ID NO. 2 and 4 that are enabled as receptors for bacterial intimin, are from EPEC and EHEC *E. coli* pathogens. Other than these two Tir polypeptides, no other Tir polypeptides from any other organism, microorganism or macroorganism, viruses, parasites, fungi, Gram positive or Gram negative bacteria, pathogenic or non-pathogenic, have been isolated, purified or characterized as receptors for any intimin. A pharmaceutical composition comprising such a Tir that is 'suitable for treating' any generic pathogen infection is not enabled. The therapeutic or prophylactic efficacy of Tir polypeptides of SEQ ID NO. 2 and 4 has not been evaluated. The statements made on pages 11-12 of the specification that Tir polypeptide 'may be produced by any organism', including *Vibrio*, *Campylobacter*, *Helicobacter*, *Pseudomonas*, *Flavobacterium*, *Haemophilus* and *Bordetella* genera, EaggEC, UPEC, *Shigella*, *Salmonella*, aerobic or anaerobic cocci etc., is merely speculative, which is unsubstantiated by concrete evidence. The specification shows that, even among the two pathogenic *E. coli* tested, i.e., EPEC and ETEC, there is variability in Tir structure and functions. Unlike EPEC, EHEC is described as not causing tyrosine phosphorylation of its Tir receptor. See the full paragraph on page 12. While EPEC-secreted Tir is described as having a molecular weight of 78 kDa by SDS-PAGE on page 14 of the specification, there is no showing that the same is true with EHEC-secreted Tir. There is absolutely no showing that any organism, or any bacterium, such as, *Vibrio*, *Campylobacter*, *Helicobacter*, *Pseudomonas*, *Flavobacterium*, *Haemophilus* and *Bordetella* genera, EaggEC, UPEC, *Shigella*, *Salmonella*, aerobic or anaerobic cocci secrete a Tir polypeptide, let alone a phosphorylated or unphosphorylated Tir polypeptide of an established molecular weight or a specific amino acid composition. A pharmaceutical composition comprising a Tir polypeptide of any one of these

microorganisms that is ‘suitable for treating’ any pathogenic infection, i.e., viral, fungal, parasitic or bacterial infection, is not enabled within the instant specification. Any Tir polypeptide, including those with the structure of SEQ ID NO: 2 and 4, have not been established to be ‘suitable for treating’ any pathogenic infection, including EHEC or EPEC infection in a suitable host. The statements made in Example XI that cattle are vaccinated with Tir to reduce the occurrence of beef contaminated by EHEC, or to even eliminate the incidence of EHEC-associated illnesses, is not substantiated by concrete evidence or data. Due to the lack of specific disclosure and/or guidance, the unpredictability factor associated with the polypeptide functions (therapeutic or prophylactic), the breadth of the claims, and the quantity of experimentation necessary, undue experimentation would have been required to practice the invention as claimed. The claims are viewed as not meeting the scope of enablement provisions of 35 U.S.C § 112, first paragraph.

11) Claims 53-59 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claims 53-59 contain new matter. Applicants point to page 34, line 16 of the specification as providing support for claims 53 and 54, i.e., a substantially purified Tir polypeptide-containing pharmaceutical composition in a delivery vehicle, such as, liposome. However, there is no descriptive support in this part of the instant specification, as originally filed, for such a pharmaceutical composition. Instead, this part of the specification recites that ‘the intimin-containing cell delivery vehicle is a liposome’.

Applicants point to page 34, lines 30 and 31, bridging to page 35, lines 1-4 of the specification as providing support for claim 55, i.e., a substantially purified Tir-polypeptide-containing pharmaceutical composition comprising a pharmaceutically acceptable carrier in a ‘unit dosage form’. However, this part of the specification describes the dosage range for the biologically active substances effective for cosmetic uses, such as, moisturizers, vitamins, perfumes etc.

Applicants point to page 50, line 28 of the specification for the limitation ‘pathogenic’. However, the sentence that appears in this part of the specification states: ‘These data indicate that these molecules and the functions they perform are critical for pathogenesis’. This does not constitute descriptive support for the new claim 59, which recites: ‘A pharmaceutical composition suitable for treating a pathogenic infection comprising the polypeptide of claim 1 and a pharmaceutically acceptable carrier’.

Applicants have not pointed to specific parts of the specification that provide descriptive support for the new claims 56-59. Therefore, the above-identified new limitations in the instant claim s are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader

original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitation(s), or to remove the new matter from the claim(s).

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

- 12)** The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

- 13)** Claims 3-7 and 52-59 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 3 is vague in the recitation 'pathogen', because the precise nature of the pathogen is not clear. Is this a viral pathogen, parasitic pathogen, fungal pathogen, or bacterial pathogen?

(b) In claims 6 and 7, in order to distinctly claim the subject matter, it is suggested that Applicants replace the limitation 'an amino acid sequence' with --the amino acid sequence--.

(c) In claim 52, for proper antecedence, it is suggested that Applicants replace the recitation 'a polypeptide of claim 1' with --the polypeptide of claim 1--.

(d) Claim 59 is vague in the recitation 'pathogenic infection', because the precise nature of the 'pathogenic infection' is not clear. Is this a viral pathogenic infection, a parasitic pathogenic infection, a fungal pathogenic infection, or a bacterial pathogenic infection?

(e) Claims 4-7 and 53-59, which depend directly or indirectly from claim 3 or claim 52, are also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, because of the vagueness or indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

- 14)** The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- 15)** Claims 1, 3-5, 52, 53, 55, 57 and 59 are rejected under 35 U.S.C. § 102(b) as being anticipated by Rosenshine *et al.* (*EMBO J.* 15: 2613-2624, 03 June 1996 – Applicants' IDS) (Rosenshine *et al.*, 1996) as evidenced by Kenny *et al.* (*Cell* 91: 511-520, 14 November 1997 – Applicants IDS).

Rosenshine *et al.* (1996) taught the Hp90 protein which associates directly with the EPEC adhesin, intimin (see abstract). Rosenshine *et al.* (1996) taught the Triton X-100-extracted Hp90protein (i.e., substantially purified) and the Hp90 protein that is separated by SDS-PAGE and immunoblotted with anti-

phosphotyrosine antibodies. The protein is contained in a Tris-HCl buffer or a desalted solution (see ‘Protein extraction and fractionation’; ‘Western immunoblotting’; and ‘Association of Hp90 with intimin on EPEC surfaces’ under ‘Materials and methods’; and Figures 2, 5 and 6). The detergent-extracted Hp90 polypeptide, resolved by SDS-PAGE, transferred to nitrocellulose, and renatured with guanidine hydrochloride bound to intimin (see page 2619, and Figures 7 and 8). The Hp90 polypeptide is co-precipitated with the intimin-maltose-binding protein (see 2619, right column) and is contained in a desalted solution, i.e., pharmaceutically acceptable carrier or a delivery vehicle (see Figure 8 legend). Rosenshine *et al.* (1996) taught that once phosphorylated, Hp90 binds to intimin (see Figure 9 legend). Rosenshine *et al.* (1996) taught that Hp90 is purified by the immunoprecipitation procedures taught in their publication (see page 2621, lines 7-10).

That the prior art Hp90 is the same as the EPEC-secreted bacterial protein, Tir, is inherent from the teachings of Rosenshine *et al.* (1996) in light of what is known in the art. For instance, Kenny *et al.* taught that Hp90 or Tir is an EPEC (i.e., A/E pathogen)-secreted protein (see abstract and first paragraph under ‘Discussion’).

Claims 1, 3-5, 52, 53, 55, 57 and 59 are anticipated by Rosenshine *et al.* (1996). The reference of Kenny *et al.* is not used as a secondary reference in combination with Rosenshine *et al.* (1996), but rather is used to show that every element of the claimed subject matter is disclosed by Rosenshine *et al.* (1996). See *In re Samour* 197 USPQ 1 (CCPA 1978).

Furthermore, the limitation “secreted by enterohemorrhagic *E. coli*” in claim 5 represents a process limitation. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown the underlying structure of the prior art polypeptide differs from that of the polypeptide claimed in claim 5.

Rejection(s) under 35 U.S.C. § 103

16) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in

section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

17) Claims 52-54, 56 and 58 are rejected under 35 U.S.C § 103(a) as being unpatentable over Rosenshine *et al.* (1996) (*EMBO J.* 15: 2613-2624, 03 June 1996 – Applicants' IDS).

Claim 52 or 53 is included in this rejection since claims 54, 56 and 58 include 'claim 52' or 'claim 53' as a limitation.

The teachings of Rosenshine *et al.* (1996) are explained above, which do not expressly disclose the Hp90 polypeptide being in a liposome, being in the form of a tablet or capsule, or in a sterile, buffered, injectible carrier.

However, formulation of an art-known protein or polypeptide as a liposome, a tablet, a capsule, or adding a sterile buffered injectible carrier to an art-known protein or polypeptide is routine and conventionally practiced in the art, especially when easy consumption or generation of antibodies is intended. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add an art-known sterile pharmaceutical, injectible buffer to the prior art Hp90 protein, or formulate it as a liposome, tablet or capsule using art-known techniques, to produce the instant invention with a reasonable expectation of success, since such a practice is routine and conventional in the art. Formulation of the claimed composition using Rosenshine's (1996) Hp90 protein is well within the realm of routine experimentation.

Claims 52-54, 56 and 58 are *prima facie* obvious over the prior art of record.

Remarks

- 18) Claims 1-7 and 52-59 stand rejected.
- 19) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.
- 20) Any inquiry concerning this communication or earlier communications from the Examiner should be

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directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

February, 2004

SD
S. DEVI, PH.D.
PRIMARY EXAMINER